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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/982,516	10/18/2001	John Madsen	05213-05621 (43170-264313)	7221

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EXAMINER

MAYES, LAURIE A

ART UNIT

PAPER NUMBER

1653

DATE MAILED: 03/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/982,516

Applicant(s)

MADSEN ET AL.

Examiner

Laurie Mayes

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 6) ☐ Other:

DETAILED ACTION

Specification

The use of the trademarks has been noted in this application (e.g., Streamline™, Sepharose™, Toyopearl™, etc.). It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johansson et al. (Journal of Biotechnology 48 (1996) pp. 9-14) in view of MacDonald et al. (Biochemical and Biophysical Research Communications, 264, pp. 469-477 (1999)). Johansson et al. teach a method of purifying recombinantly produced periplasmic protein, exotoxin A (p. 10, col. 2, 1st para.), comprising growth of the target protein (p. 10, col. 2, 1st para.), applying a mixture containing the protein to an expanded bed cation exchange Streamline™ column (p. 10, col. 2, para. 2), collecting eluate from the expanded bed cation exchange column, purifying the cells, concentrating, filtering, passing through a membrane (p. 10, col. 1, 1st para.) and applying the eluate to a Sepharose column (p. 10, col. 1, 1st para.) and later to a hydrophobic column (p. 10, col. 1, para. 2). Johansson also teaches that expanded bed adsorption chromatography could also be used as an alternative for capturing proteins otherwise capturable by centrifugation (p. 14, Johansson, col. 2, 1st para.).

MacDonald et al. teach the advantages of recombinant production of angiostatin protein such as allowing large quantities of fully defined and well characterized protein to be produced for study and the advantages of purifying proteins by expanded bed chromatography which is faster, more efficient and results in higher yields (Johansson, p. 14, col. 1, paras. 1-3). McDonald et al. also teach that angiostatin may be purified and captured by centrifugation (p. 470, col. 2, 1st para.) Therefore, given the advantages of large scale purification of angiostatin and that purification otherwise done by centrifugation, namely, purification of angiostatin, could also be purified by the more advantageous expanded bed methods, it would have been obvious to one of ordinary skill in the art at the time of the invention to use expanded bed chromatography

Art Unit: 1653

to produce high yield angiostatin protein. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, prima facie obvious.

Claims 2 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johansson et al. in view of MacDonald et al. as applied to claims 1 and 4 above, and further in view of Goldstein et al. (United States Patent Number 5,861,295). Goldstein et al. teach the purification of proteins by concentrating the proteins (col. 12, lines 55-60)(present claim 2), diafiltration (col. 12, lines 65-67)(present claim 2) and then further concentration the proteins (col. 13, lines 3-5)(present claim 2), purification by ammonium sulfate (col. 9, line 25), by hydrophobic chromatography (col. 9, lines 27-28), hydroxylapatite chromatography (col. 12, lines 25-30), by passing through more than one membrane (col. 13, lines 45-50) concentrating and pooling the fluid (col. 13, lines 57) and aseptically filtering the concentrated fluid (col. 13, lines 60-67)(present claim 2). Goldstein et al. teach that these steps prevent the contamination of the proteins during the purification process. (col. 4, lines 20-25). Given the advantages of purifying proteins without contamination as taught by Goldstein, it would have been obvious to one of ordinary skill in the art at the time of the invention by the applicant to use these step to purify recombinantly produced angiostatin. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, prima facie obvious.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Johansson et al. in view of MacDonald et al. as applied to claims 1 and 4 above, and further in view of Folkman et al. (United States Patent Number 5,837,682). Folkman et al. teach a method of expressing human angiostatin in *Pichia pastoris* (col. 40, lines 40-50) and that the advantages thereof in terms of protein processing, protein folding, and posttranslational modification inclusive of

Art Unit: 1653

glycosylation (col. 40, lines 52-55) and also teach a method of purifying recombinantly produced angiostatin comprising applying crude fermentation broth containing the recombinantly produced angiostatin and isolated over sepharose (col. 36, lines 10 and 20-30). Given the advantages of expressing human angiostatin in *P. pastoris* as taught by Folkman et al., it would have been obvious to one of ordinary skill in the art at the time of the invention by the applicant to purify recombinantly produced angiostatin that is produced from fermentation of *P. pastoris*. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, prima facie obvious.

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Johansson et al. in view of MacDonald et al as applied to claims 1 and 4 above, and further in view of Flickinger et al. (United States Patent Number 5,837,826). Flickinger et al. teach that in expanded bed chromatography used to purify proteins, it is standard that the fluid containing the protein to be purified is passed through the column in one direction and the elution buffer flow in the reverse direction (col. 6, lines 5-25). Given the benefits of following standard and known procedure for expanded bed chromatography for a successful outcome as taught by Flickinger et al., it would have been obvious to one of ordinary skill in the art at the time of the invention by the applicant to follow standard expanded bed chromatography procedures and to apply to fluid with the angiostatin to the expanded bed in an upward direction and the elution buffer in the reverse direction. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, prima facie obvious.

Art Unit: 1653

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laurie Mayes whose telephone number is (703) 605-1208. The examiner can normally be reached on Monday through Friday from 7 AM to 3:30 PM

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 305-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1123.

L. Mayes

Laurie Mayes
Patent Examiner
Art Unit 1653
March 9, 2003

Christopher S. Low

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